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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/721,091	11/26/2003	Terry J. Amiss	P-6011	6187
46851	7590	12/08/2006	EXAMINER	
DAVID W. HIGHET BECTON, DICKINSON AND COMPANY 1 BECTON DRIVE, MC110 FRANKLIN LAKES, NJ 07417			VENC, DAVID J	
			ART UNIT	PAPER NUMBER
			1641	

DATE MAILED: 12/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	10/721,091	AMISS ET AL.	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on September 22, 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 and 12-58 is/are pending in the application.
- 4a) Of the above claim(s) 19-58 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 12-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-9 and 12-58 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>09/22/06</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Examiner acknowledges Applicants' reply filed September 22, 2006.

Claims 19-58 are directed to non-elected inventions and were withdrawn from consideration in the Office Action of July 29, 2005.

Currently, claims 1-9 and 12-18 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

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Claim Rejections - 35 USC § 112

Claims 1-9 and 12-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1:

In step a), the phrase "said fusion protein has a dissociation constant of at least 1 mM towards said analyte" is indefinite because the exact experimental conditions for measurement of dissociation constants is not clear. Applicants' specification does not provide a definite standard for ascertaining the dissociation constants, such that one of ordinary skill in the art would be reasonably apprised of the scope of the invention.

In step a), the recitation of "said fusion protein has a dissociation constant of at least 1 mM towards said analyte" results in a scope mismatch in step c) wherein "said analyte is bound to said functional mutant periplasmic glucose-galactose binding protein".

In step d), the recitation of "the measured the luminescence value" appears grammatically awkward.

In claim 18, the recitation of the term "Alexa" is indefinite. The identity of "Alexa" is not clear.

Claim Rejections - 35 USC § 103

Claims 1-9, 12-13 and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellinga & Looger (US 2004/0118681) in view of Romoser *et al.*, 272 J. BIOL. CHEM. 13270 (1997).

Hellinga & Looger teach a method for quantifying an analyte (see para. [0031], “[a]ssays for ligand”) in a sample (see para. [0031], “body fluids”) comprising the steps of:

- a) administering a fusion protein (see para. [0029], “the reporter group can be present as a fusion”; para. [0030], “gene fusions”) to said sample, said fusion protein comprising a functional periplasmic binding protein (see Table 5, “glucose BP”);
- b) measuring the luminescence of said fluorescent fusion protein in the absence of analyte (see para. [0031], “[a] blank sample containing no ligand”);
- c) measuring the luminescence of said fluorescent fusion protein in the presence of analyte (see para. [0031], “[a]ssays for ligand”); and

Hellinga & Looger do not describe a detection scheme based on resonance energy transfer incorporating a “labeling moiety” and “fluorescent protein”.

However, Romoser *et al.* describe a detection scheme based on resonance energy transfer (see Abstract, “fluorescence resonance energy transfer between the two fluorophores”) incorporating a labeling moiety and fluorescent protein (see Title, “Two Green Fluorescent Protein Variants”):

It would have been obvious to a person of ordinary skill in the art to replace the detection scheme of Hellinga & Looger with a detection scheme based on resonance energy transfer between a labeling

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moiety and fluorescent protein because Romoser *et al.* discovered that such a detection scheme resulted in a 30% fractional reduction at F_{510} *in vivo* and a 65% fractional reduction at F_{510} *in vitro* (see p. 13273, right column, first full paragraph).

Claims 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellinga & Looger (US 2004/0118681) and Romoser *et al.*, 272 J. BIOL. CHEM. 13270 (1997), as applied to claims 1 and 13, and further in view of Tsien & Campbell (US 2003/0059835).

Hellinga & Looger and Romoser *et al.* teach a method for quantifying an analyte as substantially described, *supra*, and incorporated herein.

Lakowicz *et al.* do not teach a method using DsRed2(C119A).

However, Tsien & Campbell teach the use of DsRed2 (see para. [0012]), including C119 mutant DsRed (see e.g. para. [0128], "C117E"), for use as a member of a donor/acceptor pair for fluorescence resonance energy transfer (see para. [0008]).

It would have been obvious for a person of ordinary skill in the art to modify the method of Hellinga & Looger and Romoser *et al.* by using DsRed2(C119A) because Tsien & Campbell discovered the importance of C119 in fluorescent protein oligomerization. Tsien & Campbell also discovered that, by mutating key amino acid residues—including C119—oligomerization can be minimized (see e.g. para. [0128], "The ultimate product of the mutagenesis approach described herein is a monomeric red fluorescent protein"), which results in improved data interpretation (see para. [0010] – [0013]).

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Response to Arguments

Claim Rejections - 35 USC § 112

In prior Office Action, claim 1 was rejected under 35 U.S.C. 112, second paragraph, because the phrase "said fusion protein has a dissociation constant of at least 1 mM towards said analyte" is indefinite. The exact experimental conditions for measurement of dissociation constants is not clear. Applicants' specification does not provide a definite standard for ascertaining the dissociation constants, such that one of ordinary skill in the art would be reasonably apprised of the scope of the invention.

In response, Applicants cite M.P.E.P. § 2173.02 and urge Examiner to "allow the claims which define the patentable subject matter with a reasonable degree of particularity and distinctness" (see Applicants' reply, paragraph bridging 9-10) (emphasis in original).

Applicants' argument is not persuasive. Examiner has not raised the issue of a "degree" of particularity or a "degree" of distinctness and does not do so here. Examiner posits that Applicants' claim language has no particularity and no distinctness.

The following is an applicable paragraph from the M.P.E.P. 2173.05:

A claim may be rendered indefinite by reference to an object that is variable. For example, the Board has held that a limitation in a claim to a bicycle that recited "said front and rear wheels so spaced as to give a wheelbase that is between 58 percent and 75 percent of the height of the rider that the bicycle was designed for" was indefinite because the relationship of parts was not based on any known standard for sizing a bicycle to a rider, but on a rider of unspecified build. *Ex parte Brummer*, 12 USPQ2d 1653 (Bd. Pat. App. & Inter. 1989).

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Here, Applicants' recited object "dissociation constant" is a variable object. According to Uchida *et al.*, 104 J. PHYS. CHEM. 12091 (2000), fluorescent molecules have different spectral properties, depending on how they are interfaced with a detector (see Fig. 4 and Fig. 5). Examiner posits that Applicants' specification paragraph 0073-0075 reciting generic "saline solution"¹ and generic "spectrofluorometer"² provides insufficient information to a skilled artisan for establishing how Applicants' glucose-galactose binding protein was interfaced with a detector. Absent this information, Examiner posits, a hypothetical skilled artisan will not be able to meaningfully compare³ their hypothetical glucose-galactose binding protein "dissociation constant" to Applicants' recited "dissociation constant".

Claim Rejections - 35 USC § 103

In prior Office Action, claims 1-9, 12-13 and 17-18 were rejected under 35 U.S.C. 103(a) as being unpatentable over Hellinga & Looger (US 2004/0118681) in view of Romoser *et al.*, 272 J. BIOL. CHEM. 13270 (1997). In addition, claims 14-16 were rejected under 35 U.S.C. 103(a) as being unpatentable over Hellinga & Looger (US 2004/0118681) and Romoser *et al.*, 272 J. BIOL. CHEM. 13270 (1997), as applied to claims 1 and 13, and further in view of Tsien & Campbell (US 2003/0059835).

Applicants' argumentation on these issues is not persuasive. The following is an applicable generic form paragraph from the M.P.E.P.:

*...the test for obviousness is not whether the features of a secondary reference may be
bodily incorporated into the structure of the primary reference; nor is it that the claimed*

¹ To the best of Examiner's knowledge, there is no standard authority establishing the composition of a standard "saline solution". Examiner welcomes objective evidence to the contrary.

² To the best of Examiner's knowledge, there is no standard authority establishing a standard "spectrofluorometer" in Applicants' art. Examiner welcomes objective evidence to the contrary.

³ According to M.P.E.P. 2173, the primary purpose of the definiteness requirement of 35 U.S.C. 112, second paragraph, is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent.

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invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

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Conclusion

No claims are allowable at this time.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Examiner
Art Unit 1641

djv


LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600